

1 68. (Amended) The intact charge-switch NP probe according to claim 67,
2 wherein said metal ion is selected from the group consisting of Mg^{++} , Mn^{++} , K^{+} and Na^{+} .

REMARKS

Claims 1-68 are pending in this application and presented for examination. Claims 49-66 added in Applicants' response dated August 9, 2002, should have been numbered 51-68, as claims 1-50 were filed in the application. As such, these claims have been renumbered. Attached hereto is a marked-up version of the changes made to claims by the current amendment. The attached page is captioned "Version with markings to show changes made." Reconsideration is respectfully requested.

The Examiner has requested a species election between the following two groups:

(1) An NP probe having a terminal phosphate with a fluorophore moiety attached thereto wherein the charge difference between the NP probe and the phosphate detectable moiety that is cleaved from the NP probe is at least 0.5; and

(2) An intact charge-switch nucleotide phosphate (NP) probe, wherein, the phosphate detectable moiety migrates to an electrode, and the intact charge-switch NP probe migrates to the other electrode.

The Examiner alleges that claims 1-21 read on species 1 and claims 49-66 (renumbered 51-68) read on species 2. In response to the species election, Applicants elect with *traverse*, species 2 for examination proposes only.

Under MPEP § 806.04(f):

Claims to be restricted to different species must be mutually exclusive. The general test as to when claims are restricted, respectively, to different species is the fact that one claim recites limitations which under the disclosure are found in a first species but not in a second, while a second claim recites limitations disclosed only for the second species and not the first. This is frequently expressed by saying that claims to be restricted to different species must recite the mutually

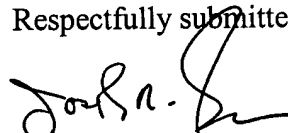
exclusive characteristics of such species.

Restriction of the invention to species 2 is improper because features found in species number 1 can be found in species number 2. For example, the compounds recited in claim 21 are within the ambit of species 1 and species 2. Moreover, many of the compounds listed in Figure 2 fall within the ambit of both species 1 and species 2. Thus, the restriction to a single species is improper, as for example, claim 21 falls within the ambit of both species.

Therefore, Applicants respectfully request that the Examiner join claims 1-21 and 49-66 (renumbered 51-68) and examine these claims on their merits.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 925-472-5000.

Respectfully submitted,



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1 51. [49.] (Amended) An intact charge-switch nucleotide phosphate (NP)
2 probe, wherein, upon enzymatic cleavage of said intact charge-switch NP probe to produce a
3 phosphate detectable moiety, said phosphate detectable moiety migrates to an electrode, and said
4 intact charge-switch NP probe migrates to the other electrode.

1 52. [50.] (Amended) The intact charge-switch NP probe according to claim
2 51. [49,] wherein either said intact NP probe has a positive molecular charge, or wherein upon
3 cleavage of said phosphate detectable moiety, said phosphate detectable moiety carries a
4 different charge relative to said intact NP probe.

1 53. [51.] (Amended) The intact charge-switch NP probe according to claim
2 51. [49,] wherein either said intact NP probe has a negative molecular charge, or wherein upon
3 cleavage of said phosphate detectable moiety, said phosphate detectable moiety carries a
4 different charge relative to said intact NP probe.

1 54. [52.] (Amended) The intact charge-switch NP probe according to claim
2 51. [49,] wherein said charge-switch NP probe is a nucleotide triphosphate (NTP); and wherein
3 said phosphate detectable moiety is a pyrophosphate with a fluorophore moiety attached thereto.

1 55. [53.] (Amended) The intact charge-switch NP probe according to claim
2 51. [52,] wherein said intact NTP probe has a positive charge.

1 56. [54.] (Amended) The intact charge-switch NP probe according to claim
2 54. [52,] wherein upon cleavage of said phosphate detectable moiety as a pyrophosphate
3 fluorophore moiety, said pyrophosphate fluorophore moiety carries a positive charge relative to
4 said intact NTP probe.

1 57. [55.] (Amended) The intact charge-switch NP probe according to claim
2 54. [52,] wherein upon cleavage of said phosphate detectable moiety as a pyrophosphate
3 fluorophore moiety, said pyrophosphate fluorophore moiety carries a negative charge relative to
4 said intact NTP probe.

1 58. [56.] (Amended) The intact charge-switch NP probe according to claim
2 51. [49,] wherein said NTP probe is a member selected from the group consisting of a
3 deoxynucleotide triphosphate (dNTP), and a nucleotide triphosphate (NTP).

1 59. [57.] (Amended) The intact charge-switch NP probe according to claim
2 58. [56,] wherein said NTP probe is a deoxynucleotide triphosphate (dNTP).

1 60. [58.] (Amended) The intact charge-switch NP probe according to claim
2 59. [57,] wherein said deoxynucleotide triphosphate (dNTP) is a member selected from the group
3 consisting of deoxyadenosine triphosphate, deoxycytosine triphosphate, deoxyguanosine
4 triphosphate deoxythymidine triphosphate and deoxyuridine triphosphate.

1 61. [59.] (Amended) The intact charge-switch NP probe according to claim
2 58. [56,] wherein said nucleotide triphosphate (NTP) is a member selected from the group
3 consisting of adenosine triphosphate, cytosine triphosphate, guanosine triphosphate and uridine
4 triphosphate.

1 62. [60.] (Amended) The intact charge-switch NP probe according to claim
2 54. [52,] wherein said fluorophore moiety is attached to said terminal phosphate via a linker.

1 63. [61.] (Amended) The intact charge-switch NP probe according to claim
2 62. [60,] wherein said fluorophore linker is an alkylene group having between about 5 to about
3 12 carbons.

1 64. [62.] (Amended) The intact charge-switch NP probe according to claim
2 62. [60,] wherein said linker carries at least one positive charge.

1 65. [63.] (Amended) The intact charge-switch NP probe according to claim
2 62 [60] wherein said linker carries at least two positive charges.

1 66. [64.] (Amended) The intact charge-switch NP probe according to claim
2 51, [49,] wherein at least one of the phosphate moieties of said nucleotide phosphate probe has
3 an ionized oxygen atom with a counter-cation associated therewith.

1 67. [65.] (Amended) The intact charge-switch NP probe according to claim
2 51, [49,] wherein said counter-cation is a metal ion.

1 68. [66.] (Amended) The intact charge-switch NP probe according to claim
2 67, [65,] wherein said metal ion is selected from the group consisting of Mg^{++} , Mn^{++} , K^{+} and
3 Na^{+} .